Please cancel the paragraph on page 2, line 33, through page 3, lines 1-2, and replace it with the following:

B2

After previously being considered as just a biologically inactive tissue component compressing the spinal nerve root at disc herniation, the nucleus pulposus has recently been found to be highly active, inducing both structural and functional changes in adjacent nerve roots when applied epidurally (24, 37, 38, 41, 42). It has thereby been established that autologous nucleus pulposus may induce axonal changes and a characteristic myelin injury (24, 38, 41, 42), increased vascular permeability (9, 44), intra vascular coagulation (24, 36), and that membrane-bound structure or substances of the nucleus pulposus-cells are responsible for these effects (24, 37). The effects have also been found to be efficiently blocked by methyl-prednisolone and cyclosporin A (2, 38). When critically looking at these data, one realizes that there is at least one cytokine that relates to all of these effects, Tumor Necrosis Factor alpha (TNF-α). Further, the active component comprises a substance inhibiting a compound triggered by the release of TNF-α, such as interferon-gamma, interleukin-1, and nitrogen oxide (NO) in the form of base or addition salts.

Please cancel the paragraph beginning on Page 4, line 24 and which continues to Page 5, Line 5 and replace it with the following:

B3

After previously being considered as just a biologically inactive tissue component compressing the spinal nerve root at disc herniation, the nucleus pulposus has recently been found to be highly active, inducing both structural and functional changes in adjacent nerve roots when applied epidurally (24, 37, 38, 41, 42). It has thereby been established that autologous nucleus pulposus may induce axonal changes and a characteristic myelin injury (24, 38, 41, 42), increased vascular permeability (9, 44), intra vascular coagulation (24, 36), and that membrane-bound structure or substances of the nucleus pulposus-cells are responsible for these effects (24, 37). The effects have also been found to be efficiently

B3 Cont'd

blocked by methyl-prednisolone and cyclosporin A (2, 38). When critically looking at these data, one realizes that there is at least one cytokine that relates to all of these effects, Tumor Necrosis Factor alpha (TNF-α). To assess if TNF-α may be involved in the nucleus pulposus induced nerve root injury, the presence of TNF-α in nucleus pulposus-cells was assessed by studying if the nucleus pulposus-induced effects could be blocked by doxycycline, a soluble TNF-receptor, and a selective monoclonal TNF-antibody. The latter was administered both locally in the nucleus pulposus and systemically.

Please cancel the paragraph on page 6, lines 14-21, and replace it with the following:

B4

Nucleus pulposus was harvested from the 5th lumbar disc through a retro peritoneal approach (42). Approximately 40 mg of the nucleus pulposus was applied to the sacrococcygeal cauda equina through a midline incision and laminectomy of the first coccygeal vertebra. Four pigs did not receive any treatment (no treatment). Four other pigs received an intravenous infusion of 100 mg of doxycycline (Vibramycino, Pfizer Inc., New York, USA) in 100 ml of saline over 1 hour. In 5 pigs, the nucleus pulposus was mixed with 100 μl of a 1.11 mg/ml suspension of the anti-TNF-α antibody used in Series 1, before application.